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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/686,529	10/16/2003	Homme W. Hellinga	GRT/1579-863	4003

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EXAMINER	
ZEMAN, ROBERT A	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/686,529	HELLINGA ET AL.	
	Examiner	Art Unit	
	ROBERT A. ZEMAN	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,7-20,22-28,31 and 32* is/are pending in the application.

4a) Of the above claim(s) *16-20 and 24-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,7-15,31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5-9-2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 10-10-2007 has been entered.

The amendment and response filed on 3-13-2008 are acknowledged. Claims 7 and 8 have been amended. Claims 3-6, 21-23 and 29-30 have been canceled. Claims 31 and 32 have been added. Claims 1-2, 7-20, 24-28 and 31-32 are pending. Claims 16-20 and 24-28 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

Claims 1, 2, 7-15 and 31-32 are currently under examination.

Information Disclosure Statement

The Information Disclosure Statement filed on 5-9-2008 has been considered. An initialed copy is attached hereto.

Claim Rejections Withdrawn

The rejection of claims 1 and 3-15 under 35 U.S.C. 102(e) as being anticipated by Amiss et al. (US 2003/0134346) is withdrawn in lieu of the rejection set forth below.

The rejection of claims 1 and 3-15 under 35 U.S.C. 102(e) as being anticipated by Amiss et al. (US Patent 6,855,556) is withdrawn in lieu of the rejection set forth below.

Claim Rejections Maintained

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The rejection of claims 1-2, 7-15 and 31-32 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,277,627 is maintained for reasons set forth in the previous Office action in the rejection of claims 1-15. The cancellation of claims 3-6 has rendered the rejection of those claims moot.

Applicant argues:

1. There is no motivation given as to why the skilled artisan would have attached one or more reporter groups at positions 10, 93 or 183.

2. Mutations recited in claim 12 of the '627 patent were not made to attach a reporter group.

Applicant's arguments have been fully considered and deemed non-responsive.

With regard to Point 1 since the cited patented claims encompass all possible attachment positions within the GBP and the disclosure of the cited patent contemplates the same (see column 4-5), the specific positions recited in the instant claims are deemed to be obvious variations of the patented biosensors. Moreover, the specification of U.S. Patent 6,277,627 specifically discloses that the reporter groups can be within the ligand-binding pocket (i.e. can be an endosteric site) [see column 4, lines 21-22).

With regard to Point 2, claim 12 was the basis of the rejection.

As outlined previously, although the conflicting claims are not identical, they are not patentably distinct from each other because both claims sets are drawn to biosensors comprising a bPGP and a reporter group wherein said reporter group is attached to the GBP and can constitute a fluorophore or a redox cofactor. Moreover, since the cited patented claims encompass all possible attachment positions within the GBP and the disclosure of the cited patent contemplates the same (see column 4-5), the specific positions recited in the instant claims are deemed to be obvious variations of the patented biosensors.

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 7-15 and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hellinga (WO 99/34212 – IDS filed 3-14-2005) for the reasons set forth in the previous Office action in the rejection of claims 1-15. The cancellation of claims 3-6 has rendered the rejection of those claims moot.

Applicant argues:

1. The instant invention is directed to biosensors in which at least one reporter group is attached at one or more of amino acid positions 10, 93 or 183 of a glucose binding protein.

2. Hellinga does not teach or suggest attaching at least one reporter group to these specific positions.

3. Attaching a reporter group at amino acid position 183 provides the unexpected results of decreased binding affinity for glucose and increased fluorescence which is not taught or suggested by the art.

4. There is not expectation of success

Applicant's arguments have been fully considered and deemed non-persuasive. With regard to Point 2 and 4, Hellinga also discloses that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see column 4 lines 21-48). Moreover, Hellinga discloses that the binding protein can be mutated either within the binding site or at allosteric sites (see page 10, lines 14-17). While Hellinga does not explicitly disclose the attachment of the reporter group(s) at positions 10, 93 or 183, he does disclose that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see page 9, line 13 to page 10, line 14). Given that the attachment of reporter groups is well known in the art yielding predictable results, it is obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Hellinga attaching a reporter group both within and outside of the binding sites (see Examples 1 and 2), the skilled artisan would have had a reasonable expectation of success.

With regard to Point 3, the biosensor with a reporter group at position 183, which is encompassed by Hellinga in light of KSR, would necessarily have the same biochemical properties as that of the instant invention.

With regard to Point 4, Hellinga discloses that GBP is a member of a superfamily of receptor proteins and that their invention is not limited to the said "individual embodiments (see

page 7, lines 11-14). Consequently, it would have been obvious to the skilled artisan to apply the teachings of Hellinga et al. to use other members of said receptor superfamily with a reasonable expectation of success.

Hellinga discloses biosensors comprising glucose binding proteins (GBP) and reporter groups wherein said GBP include mutations that allow site-specific introduction of the environmentally sensitive reporter group (see abstract). Hellinga further discloses that said reporter groups can be site-specifically introduced by total synthesis, semi-synthesis or gene fusion (see page 7, lines 18-19) and that a variety of reporter groups can be used a fluorophores and redox cofactors (see page 8 lines 3-7 and claims 4-5). Hellinga also discloses that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see page 9, line 13 to page 10, line 14). Moreover, Hellinga discloses that the binding protein can be mutated either within the binding site or at allosteric sites (see page 10, lines 14-17).

The disclosure of Hellinga differs from the instant invention in that they don't specifically exemplify any other bPBP other than GBP. Moreover, they do not explicitly disclose the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14.

The disclosure of Hellinga differs from the instant invention in that they don't specifically exemplify the attachment of the reporter groups to positions 10, 93 or 183 of the glucose binding protein. Moreover, he does not explicitly disclose the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14.

However, Hellinga discloses that the strategy for introducing reporter groups into the exemplified GBP was successfully used with MBP and PBP. Consequently it would have been

obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Hellinga attaching a reporter group both within and outside of the binding sites (see Examples 1 and 2), the skilled artisan would have had a reasonable expectation of success.

With regard to the to the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14, it is deemed in the absence of evidence to the contrary, that since the biosensors disclosed by Hellinga and those of the instant invention are the same they would necessarily have the same biochemical properties.

Claims 1-2, 7-15 and 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hellinga (U.S. Patent 6,277,627 – IDS filed 3-14-2005) for the reasons set forth in the previous Office action in the rejection of claims 1-15. The cancellation of claims 3-6 has rendered the rejection of those claims moot.

Applicant argues:

1. The instant invention is directed to biosensors in which at least one reporter group is attached at one or more of amino acid positions 10, 93 or 183 of a glucose binding protein.
2. Hellinga does not teach or suggest attaching at least one reporter group to these specific positions.
3. Attaching a reporter group at amino acid position 183 provides the unexpected results of decreased binding affinity for glucose and increased fluorescence which is not taught or suggested by the art.
4. There is not expectation of success

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Point 2 and 4, Hellinga also discloses that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see column 4 lines 21-48). Moreover, Hellinga discloses that the binding protein can be mutated either within the binding site or at allosteric sites (see column 4, lines 49-53). While Hellinga does not explicitly disclose the attachment of the reporter group(s) at positions 10, 93 or 183, he does disclose that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see column 4 lines 21-48). Given that the attachment of reporter groups is well known in the art yielding predictable results, it is obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Hellinga attaching a reporter group both within and outside of the binding sites (see Examples 1 and 2), the skilled artisan would have had a reasonable expectation of success.

With regard to Point 3, the biosensor with a reporter group at position 183, which is encompassed by Hellinga in light of KSR would necessarily have the same biochemical properties as that of the instant invention.

With regard to Point 4, Hellinga discloses that GBP is a member of a superfamily of receptor proteins and that their invention is not limited to the said "individual embodiments (see page 7, lines 11-14). Consequently, it would have been obvious to the skilled artisan to apply the teachings of Hellinga et al. to use other members of said receptor superfamily with a reasonable expectation of success.

Hellinga discloses biosensors comprising glucose binding proteins (GBP) and reporter groups wherein said GBP include mutations that allow site-specific introduction of the environmentally sensitive reporter group (see abstract). Hellinga further discloses that said reporter groups can be site-specifically introduced by total synthesis, semi-synthesis or gene fusion (see column 1, lines 46-48) and that a variety of reporter groups can be used a fluorophores and redox cofactors (see column 3, lines 48-52 and claims 4-5). Hellinga also discloses that said reporter groups can be positioned in the binding pocket (ligand binding pocket) or distally from the binding pocket (see column 4 lines 21-48). Moreover, Hellinga discloses that the binding protein can be mutated either within the binding site or at allosteric sites (see column 4, lines 49-53).

The disclosure of Hellinga differs from the instant invention in that they don't specifically exemplify the attachment of the reporter groups to positions 10, 93 or 183 of the glucose binding protein. Moreover, he does not explicitly disclose the specific $\Delta I_{std\ or}\ \Delta R_{max}$ values recited in claims 11-14.

However, Hellinga discloses that the strategy for introducing reporter groups into the exemplified GBP was successfully used with MBP and PBP. Consequently it would have been obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Hellinga attaching a reporter group both within and outside of the binding sites (see Examples 1 and 2), the skilled artisan would have had a reasonable expectation of success.

With regard to the to the specific $\Delta I_{std\ or}\ \Delta R_{max}$ values recited in claims 11-14, it is deemed in the absence of evidence to the contrary, that since the biosensors disclosed by Hellinga and those of the instant invention are the same they would necessarily have the same biochemical properties.

New Grounds of Rejection

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-2 and 7-14 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-2 and 7-14 of copending Application No. 11/785,591. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 15 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/785,591. Although the conflicting claims are not identical, they are not patentably distinct from each other because both claims are drawn to biosensors comprising glucose binding proteins with a reporter group attached to position 183.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 7-15 and 31-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 7 and 8 are rendered vague and indefinite by the use of term "...position 183 of said GBP..." Given that there is no base sequence recited in the claim it is impossible to determine what specific amino acid is being claimed. Applicant has previously argued (see response filed on 8-23-2006), that the base sequence is the GBP amino acid sequence

incorporated by reference from U.S. Patent 6,277,627. However, there is no specific reference to said sequence in the rejected claim. Applicant is reminded that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Claim 15 is rendered vague and indefinite by the use of term "...positions of said GBP selected from the group consisting of 10, 93 and 183." Given that there is no base sequence recited in the claim it is impossible to determine what specific amino acid is being claimed. Applicant has previously argued (see response filed on 8-23-2006), that the base sequence is the GBP amino acid sequence incorporated by reference from U.S. Patent 6,277,627. However, there is no specific reference to said sequence in the rejected claim. Applicant is reminded that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

35 USC § 103

Claims 1 and 73-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amiss et al. (US 2003/0134346).

Amiss et al. disclose biosensors comprising galactose/glucose binding proteins (GGBP) and reporter groups wherein said GGBP includes at least on mutation and at least one reporter group (paragraph 0017). Amiss et al. further disclose that mutations of binding proteins include the addition or substitution of cysteine groups, non-naturally occurring amino acids and replacement of substantially non-reactive amino acids with reactive amino acids to provide for

the covalent attachment of electrochemical or photoresponsive reporter groups (see paragraph 0025) and that a variety of reporter groups can be used such as fluorophores (e.g. acrylodan - see paragraph [0031]) and redox cofactors (see paragraph [0032]). Amiss et al. also disclose that said reporter groups can be attached to the GGBPs by any conventional means throughout the length of the protein. (see paragraph 0034). It should be noted that while Amiss et al. do not explicitly disclose the attachment of the reporter group(s) at positions 10, 93 or 183, Amiss does disclose that said reporter groups can be attached covalently to cysteine residues. Given that the attachment of reporter groups is well known in the art yielding predictable results, it is obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Amiss attaching a reporter group to positions 11, 14, 19, 43, 74, 07, 110, 110, 112, 113, 137, 149, 152, 153, 213, 216, 238, 287 and 292, the skilled artisan would have had a reasonable expectation of success.

With regard to the to the specific ΔI_{std} or ΔR_{max} values recited in claims 11-14, it is deemed in the absence of evidence to the contrary, that since the biosensors disclosed by Amiss et al. are and those of the instant invention are the same they would necessarily have the same biochemical properties.

Claims 1 and 73-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amiss et al. (US Patent 6,855,556)

Amiss et al. disclose biosensors comprising galactose/glucose binding proteins (GGBP) and reporter groups wherein said GGBP includes at least on mutation and at least one reporter group (column 3, lines 44-50). Amiss et al. further disclose that mutations of binding proteins

include the addition or substitution of cysteine groups, non-naturally occurring amino acids and replacement of substantially non-reactive amino acids with reactive amino acids to provide for the covalent attachment of electrochemical or photoresponsive reporter groups (see column 5, lines 1-7) and that a variety of reporter groups can be used such as and redox cofactors (see column 6, lines 55-59). Amiss et al. also disclose that said reporter groups can be attached to the GGBPs by any conventional means throughout the length of the protein (see column 6 line 65 to column 7, line 8). It should be noted that while Amiss et al. do not explicitly disclose the attachment of the reporter group(s) at positions 10, 93 or 183, Amiss does disclose that said reporter groups can be attached covalently to cysteine residues. Given that the attachment of reporter groups is well known in the art yielding predictable results, it is obvious for the skilled artisan to utilize any or all of the possible binding sites. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]). Given the success of Amiss attaching a reporter group to positions 11, 14, 19, 43, 74, 07, 110, 110, 112, 113, 137, 149, 152, 153, 213, 216, 238, 287 and 292, the skilled artisan would have had a reasonable expectation of success.

With regard to the to the specific $\Delta I_{std\ or}$ ΔR_{max} values recited in claims 11-14, it is deemed in the absence of evidence to the contrary, that since the biosensors disclosed by Amiss et al. are and those of the instant invention are the same they would necessarily have the same biochemical properties.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT A. ZEMAN whose telephone number is (571)272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m. .

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert A. Zeman/
Primary Examiner, Art Unit 1645
June 19, 2008